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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,446	07/29/2003	Navin Vaya	1296-015	7784

47888 7590 06/14/2010

HEDMAN & COSTIGAN, P.C.
1230 AVENUE OF THE AMERICAS
7th floor
NEW YORK, NY 10020

EXAMINER	
MERCIER, MELISSA S	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
06/14/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/630,446	VAYA ET AL.	
	Examiner	Art Unit	
	MELISSA S. MERCIER	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-7,11-15,18-20,23,26,27,30-32,52,55,57,58 and 60-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-7,11-15,18-20,23,26,27,30-32,52,55,57,58 and 60-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DoongDoing wellDETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 12, 2010 has been entered.

Summary

Receipt of Applicants Remarks and Amended Claims filed on April 12, 2010 is acknowledged. Claims 1, 5-7, 11-15, 18-20, 23, 26-27, 27, 30-32, 52, 55, 57-58, 60-75 remain pending in this application. Claims 30-31 and 73-74 remain withdrawn from consideration as reading on non-elected species.

Specification

The amendment to the specification has been entered.

Withdrawn Rejections/Objections

Claim Rejections - 35 USC § 112

The rejection of claims 1, 11, 18-19, 33, 43, and 50-51 under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly

claim the subject matter which applicant regards as the invention has been withdrawn in view of Applicants Amendments to the claims adopting the Examiners suggestion regarding the weight ratios.

Maintained Rejections/Objections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-7, 13, and 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant has not particularly pointed out what is meant by claiming ammonio methacrylate copolymers type A and B as described in the USP and methacrylic acid copolymer type A, B, and C, as described in the USP. The claims must be presented to define the invention within the metes and bounds of the specification. The citation to outside sources is outside the specification.

Response to Arguments

Applicant has amended one of the claims to remove references to outside sources but has not amended the recited claims. It is suggested that in order to overcome the rejection of claim the above cited claims, Applicant thoroughly review and amend the claims in order to remove any reference to outside sources.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 5-7, 11-15, 18-20, 23, 26-27, 27, 30-32, 52, 55, 57-58, and 60-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Timmins et al. (US Patent 6,660,300) in view of Boswell (US Patent 3,048,526).

Timmins discloses a controlled release delivery system for pharmaceuticals which have high water solubility, such as antidiabetic metformin HCl salt. The delivery system includes (1) an inner solid particulate phase formed of substantially uniform granules containing a pharmaceutical having a high water solubility, and one or more hydrophilic polymers, one or more hydrophobic polymers and/or one or more hydrophobic materials such as one or more waxes, fatty alcohols and/or fatty acid esters, and (2) an outer solid continuous phase in which the above granules of inner solid particulate phase are embedded and dispersed throughout, the outer solid continuous phase including one or more hydrophobic polymers, one or more hydrophobic polymers and/or one or more hydrophobic materials such as one or more waxes, fatty alcohols and/or fatty acid esters, which may be compressed into tablets (abstract). Timmins discloses high water solubility to be solubility in water at ambient temperature of at least about 50mg/mL water (column 9, lines 40-46).

The inner solid particulate phase may comprise 10-98% drug (column 9, lines 59-61). The extended release material in the form of hydrophobic polymers and/or other hydrophobic materials is in the range of about 5-95% by weight, based on the weight of

the inner solid particulate phase (column 9, lines 62-67), which reads on the claimed weight ratio of drug: polymer particles of 100:2.5 to 100:30 as recited in the instant claims.

The inner solid particulate phase is in a weight ratio to the outer solid continuous phase is within the range of 0.5:1 to 4:1 (column 9, lines 54-58), which reads on the claimed weight ratio of particles: coating of 100:2.5 to 100:30 as recited in the instant claims.

The metformin may be used in combination with another anti-hyperglycemic and/or hypolipidemic agent within the same dosage unit in a weight ratio from about 0.01:1 to about 300:1 (column 12, lines 24-32).

Regarding claims 55, and 68-69, Suitable additional anti-hyperglycemic drugs include glyburide, glimepiride, glipizide, gliclazide, chlorpropamide, acarbose, miglitol, or thiazolidinediones including rosiglitazone, for example (column 12, line 47-column 13, line 44).

Regarding claims 5-6, 12-13, hydrophobic polymers which may be employed in the inner solid particulate phase and/or outer solid continuous phase include, but are not limited to ethyl cellulose, hydroxyethylcellulose, ammonio methacrylate copolymer, methacrylic acid copolymers, methacrylic acid-acrylic acid ethyl ester copolymer, methacrylic acid esters neutral copolymer, dimethylaminoethylmethacrylate-methacrylic acid esters copolymer, vinyl methyl ether/maleic anhydride copolymers, their salts and esters (column 10, lines 44-55).

Regarding claims 14-15 other hydrophobic materials which may be employed in the inner solid particulate phase and/or outer solid continuous phase include, but are not limited to waxes such as beeswax, carnauba wax, microcrystalline wax, and ozokerite; fatty alcohols such as cetostearyl alcohol, stearyl alcohol; cetyl alcohol and myristyl alcohol; and fatty acid esters such as glyceryl monostearate, glycerol monooleate, acetylated monoglycerides, tristearin, tripalmitin, cetyl esters wax, glyceryl palmitostearate, glyceryl behenate, and hydrogenated castor oil (column 10, lines 56-65).

Regarding claims 23 and 57-61, highly water soluble drugs, such as metformin, will be employed in a dosage range of 150-3000mg on a regimen in single daily doses or 2-4 divided daily doses, 1-4 times a day (column 20, lines 21-28).

Applicants attention is drawn to the table on the top of column 21 and Examples 1-4, which discloses 28-39% released at 1 hour, and between 75.7 through 93.1 at 6hrs (columns 21-23: Examples 1-4). Since the prior art discloses the same composition as the instant claims, it is the position of the examiner that it would possess the same functional properties at the instant claims, with regard to plasma concentrations.

Timmins does not disclose the top surface of the tablet not being covered by the outer portion.

Boswell disclosed medicinal tablet preparation containing substantially segregated quantities of the same or different ingredients (column 1, lines 7-10). Inlay tablets are disclosed (column 2, line 62-column 3, line 68).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Timmins with the tablet of Boswell in order to provide sustained-release of an active pharmaceutical with immediate release of another or the same active pharmaceutical.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have optimized the ratio of particles to coating in order to alter the drug release profile. Timmins discloses, in a controlled release dosage form, the formulator tries to reduce the rate of dissolution by, for example, embedding the drug in a polymeric matrix or surrounding it with a polymeric barrier membrane through which drug must diffuse to be released for absorption. To reduce the rate of release of drug from the dosage form to an appropriate level consistent with the blood level profile desired for a drug possessing very high water solubility, very large amounts of polymer would be required for the matrix or barrier membrane. If the total daily dose of drug to be delivered is of the order of only a few milligrams this may be feasible, but many drugs having the solubility properties described require total daily doses of the order of many hundreds of milligrams. Whilst it is possible to create oral controlled release dosage forms for such products by use of large amounts of polymer, an unacceptably large dosage form may result (column 2, lines 16-33).

Applicant is reminded that where the general conditions of the claims are met, burden is shifted to applicant to provide a patentable distinction. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. See In re Aller, 220 F.2d 454

105 USPQ 233,235 (CCPA 1955). The optimization of the polymer coating would be a rate limiting/controlling variable.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicant argues:

***Timmins requires the use of a hydrophilic polymer.**

The Examiner respectfully disagrees. Applicant's attention is directed to column 8, lines 29-45, which recite as component (b) an extended release material formed of one or more hydrophilic polymers **and/or** one or more hydrophobic polymers **and/or** one or more other type of hydrophobic materials, such as waxes, fatty alcohols, and/or fatty acid esters. While it is acknowledged, the hydrophilic polymers may be added, they are not required.

***Timmins final dosage form would be unappealing due to its size.**

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., final size of the dosage unit) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

***Timmins discloses a much higher percentage of polymer that in the instant claims.**

Timmins discloses the inner solid particulate phase may comprise 10-98% drug (column 9, lines 59-61). The extended release material in the form of hydrophobic polymers and/or other hydrophobic materials is in the range of about 5-95% by weight, based on the weight of the inner solid particulate phase (column 9, lines 62-67), which reads on the claimed weight ratio of drug: polymer particles of 100:2.5 to 100:30 as recited in the instant claims.

The inner solid particulate phase is in a weight ratio to the outer solid continuous phase is within the range of 0.5:1 to 4:1 (column 9, lines 54-58), which reads on the claimed weight ratio of particles: coating of 100:2.5 to 100:30 as recited in the instant claims.

The recited claims within Timmins overlap the ratios of the instant claims.

***Timmins does not disclose any enabled examples comprising additional antihyperglycemic compounds.**

Applicant is reminded that a patent is presumed enabled for all that it discloses. While there may be no direct example of a composition comprising two different antihyperglycemic compounds, Timmins discloses that they can be used. Applicant has not provided any evidence that the teachings of Timmins are not enabled for such a combination.

***The teachings of Boswell do not disclose a compact sustained release dosage form of high dose, highly soluble drugs in combination with low dose active.**

It is respectfully submitted that Boswell is not relied on for the teachings of the high dose, highly soluble drugs in combination with low dose active but rather that the inlay dosage form is known in the art.

***Applicant has additionally presented photos of the instantly claimed tablet and the tablet of Timmins.**

It is unclear to the Examiner what argument Applicant is attempting to make with the tablet pictures. Clarification is requested. Applicant has previously argued that the Timmins final product size is larger than the instantly claimed tablet; however, as discussed above, such a limitation is not in the claims.

Newly Applied Objections/Rejections

Claim Objections

Claim 12 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1, from which claim 12 directly depends, recites the coating on the micromatrix particles comprises one ore ore hydrophobic agents in a specific weight ratio. Whereas, claim 12 also recites the coating comprising a hydrophobic agent without a weight ratio, thereby expanding the scope of the claim.

Claim 32 and 72 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 has employed consisting of language to limit the outer portion to a high dose active agent and a hydrophobic release controlling agent, therefore, it is improper to add in additional agents, including additional active agent since it expands the scope of the claim.

Claim 55 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Applicant has limited the high dosage high solubility active agents to be selected from the group consisting of metformin hydrochloride, phenformin, and buformin, which are biguanides, however, there are also biguanides which are not metformin hydrochloride, phenformin, and buformin, thereby expanding the scope of the claim.

Claim 73* objected to because of the following informalities: it is noted that Applicant has presented a new claim numbered as 73; however, the application already contained 74 claims. This appears to be a typographical error and should have been numbered claim 75. Appropriate correction is required. For purposes of this office action, the second claim 73 will be referred to as claim 75.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1, 5-7, 11-15, 18-20, 23, 26-27, 27, 30-32, 52, 55, 57-58, and 60-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 75 recites in the preamble the dosage form comprises a high dose high solubility active ingredient as a modified release formulation as a coating over a core comprising a low dose active ingredient as an immediate release formulation. However, Applicant has amended the claim to recite the outer coating comprises micro matrix particles which consist of the high dose high solubility active and one or more hydrophobic release controlling agents in a specific ratio AND the low dose active, which is also specified. This appears to a new structural formulation and contradictory to what the entire prosecution history of this application as well as all the entire application family and would constitute new matter since this type of structural configuration is not disclosed in the specification. This does, however, appear to the Examiner to be a typographical error and the claim language was intended to recite wherein clauses for the identification of the low dose active and the high dose actives, to appear after the (a) and (b) structural elements. It is suggested Applicant contact the Examiner in order to clarify the claim language.

Further regarding claim 1, Applicant has recited a Markush Grouping for the Identification of the low dose active agent; however, Applicant has used comprising language for the Markush Grouping. Therefore, Applicant has not expressly pointed out what is to be included within the Markush Group. The Examiner has interpreted

comprising to be similar or equivalent to "such as" and indicates examples of suitable components, but not limited to such components. It is suggested Applicant amend the claims to recite "selected from the group consisting of".

Regarding claims 5 and 15, Applicant attention is directed to the suggestions above regarding the recitation of "comprising" in a Markush Grouping.

Regarding claims 20, 23, 52, and 57 Applicant has not particularly pointed out what the limitation of the dosing range actually is. Applicant has again employed comprising language, which is open ended and would allow for any dosage amount as long as it would encompass amounts within the cited range. For example, 100mg comprises 50mgs.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA S. MERCIER whose telephone number is (571)272-9039. The examiner can normally be reached on 8:00am-4:30pm Mon through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melissa S Mercier/
Examiner, Art Unit 1615

/Carlos A. Azpuru/
Primary Examiner, Art Unit 1615